Introduction

As society ages and the use of percutaneous coronary interventions increases, the preoperative condition of candidates for coronary artery bypass grafting (CABG) is becoming increasingly complex. The number of patients with severe atherosclerosis has also recently increased. Severe atherosclerotic disease has been identified as an independent risk factor for mortality and stroke\(^1,\)\(^2\) in patients undergoing coronary revascularization, and can be associated with an operative mortality as high as 14.3%.\(^3\) Careful choice of surgical techniques might reduce the risk of neurologic events in these patients. Off-pump coronary artery bypass (OPCAB) has gained worldwide popularity.\(^4\),\(^5\) Comparative reports demonstrate significant reductions in mortality and major neurologic events following the use of OPCAB.\(^6\),\(^7\) In this study, we compared the outcomes of CABG in patients with and without severe atherosclerosis. We investigated the hypothesis that different surgical techniques might prevent neurologic events and reduce mortality in those with severe atherosclerosis.
**Patients and Methods**

**Patients**

The final study population consisted of consecutive male and female patients who underwent elective isolated CABG at Kochi Health Sciences Center (Kochi, Japan) between January 2005 and September 2008. We compared the outcomes between patients with (group A) and those without (group N) severe atherosclerotic disease.

As a retrospective study, this study did not require approval by our Institutional Review Board.

A total of 373 patients underwent CABG at our institution between January 2005 and September 2008. Elective isolated CABG was performed in 225 consecutive patients; they comprised the final study group. OPCAB was performed in 212 patients (94.2%). Preoperative and intraoperative screening identified 42 (18.7%) patients with severe atherosclerotic disease (group A). They were compared with those in group N (patients without atherosclerotic disease; n = 183, 81.3%).

**Screening for atherosclerotic disease**

We evaluated atherosclerotic lesions in all patients using routine, preoperative cervical vessel echography, thoracicoabdominal computed tomography (CT), and intraoperative epiaortic echography. Patients were diagnosed with severe atherosclerotic disease (group A) if they met any of the following criteria:

i. Carotid artery with severe stenosis (>70%) measured by the NASCET (North American Symptomatic Carotid Endarterectomy Trial) method.8)

ii. Ascending aorta or aortic arch with an atherosclerotic lesion so severe that it was difficult and risky to maneuver it. Mild atheroma was defined as a localized atherosclerotic thickening of <3 mm, moderate atheroma as atherosclerotic thickening between 3–5 mm, and severe atheroma as atherosclerotic thickening >5 mm. Protruding or mobile plaques were recorded separately. We defined significant atheromatous disease (moderate-severe) as severe atherosclerotic disease.9)

iii. Severe atherosclerotic lesion in the descending aorta, iliac arteries, or femoral arteries. In these cases, it was judged impossible to cannulate the extracorporeal circulation or perform intra-aortic balloon pumping (IABP) without undue risk.

Intraoperative examination of the ascending to the descending aorta was routinely performed by both transthoracic echocardiography (TTE) and epiaortic echography. When the patient had severe atherosclerosis of the ascending aorta on TEE, echocardiography and manual palpation were performed to evaluate potential sites for arterial cannulation and side clamp application. In cases of an ascending aorta with a severe atherosclerotic lesion, we used a no-touch aorta technique and selected axillary cannulation if extracorporeal circulation was necessary. We used the method described by Wareing et al.9) to classify and grade the severity of aortic atheromas.

**Surgical procedures in coronary artery bypass grafting**

The surgical methods did not change during the study. The majority of cases involved the use of our original OPCAB technique; this approach has been previously described; a series of techniques and instruments were developed to provide access to the circumflex area while hemodynamic stability was preserved, including the left pericardial traction technique, compression of the right pericardium, and a right sternal retractor.9) We used cardiopulmonary bypass (CPB) in a standardized fashion, with a membrane oxygenator and a roller pump to perform OPCAB. We anastomosed proximal side under side aortic clamping, but we had no cross-clamping. No conventional CABG was performed in this study. All patients received 100 mg/day of aspirin before surgery; some also received clopidogrel (Plavix; Bristol-Myers Squibb/Sanofi Pharmaceuticals Partnership). All antiplatelet drugs were administered until surgery. Warfarin (Coumadin; Bristol-Myers Squibb, Princeton, New Jersey, USA) was titrated postoperatively to an international normalized ratio (INR) goal of 1.7–2.2. Many patients received continuous intravenous heparin (Hep-Lock, Liquaemin; Celsus Laboratories, Inc., Cincinnati, Ohio, USA) from the day after surgery until a target INR of 1.7 was achieved.

**Diagnosis of brain infarction**

Stroke was defined as the event of any new global or focal neurological deficit of presumed vascular origin lasting more than 24 h that could be evident soon after emergence from anesthesia (early stroke) or after first awaking without any neurological deficits (delayed stroke) until hospital discharge. A cerebrovascular accident diagnosed clinically either by an intensivist or neurologist was always confirmed by CT or magnetic resonance imaging. Stroke etiologies were identified and classified as either thromboembolism or hypoperfusion.
Patient data were collected retrospectively. Continuous variables are reported as means ± SD. Univariate analysis was carried out using the χ² test to determine significant differences. Fisher’s exact test was used to analyze between-group differences in categorical variables. Statistical significance was set at p < 0.05. We used SPSS version 11.0 (SPSS Inc, Chicago, IL, USA) to perform statistical analyses.

**Results**

Preoperative demographics and cardiovascular risk factors are listed in Table 1. Group A had significantly more patients aged >75 years. Both groups were predominantly male, and almost 40% of patients had diabetes mellitus. In group A, four (9.5%) patients were receiving hemodialysis; this was not significantly different from group N. Poor left ventricular ejection function (<50%) was present in six (14.3%) and 24 (13.1%) patients in groups A and N, respectively. The logistic EuroSCORE was significantly higher in group A than in group N (5.39 ± 2.9 vs. 3.16 ± 2.2, p < 0.001).

Surgical characteristics are shown in Table 2. OPCAB was performed in 36 of 42 patients (85.7%) in group A, and 176 of 183 patients (96.2%) in group N; on-pump CABG was performed in 6 group A patients. The aorta no-touch technique was used more frequently in group A compared with group N [27 (64.3%) vs. 74 (40.4%); p < 0.001]. In group A, axillary artery cannulation was performed in four of the six cases of CABG with on-pump beating. The mean numbers of distal anastomoses were 2.6 in group A and 3.0 in group N.

Postoperative complications and in-hospital mortality are shown in Table 3. All patients were in sinus rhythm on preoperative electrocardiogram. Postoperative atrial fibrillation occurred in six (14.3%) patients in group A compared with 23 (12.6%) in group N; the difference was not significant. Patients in group A were more likely to have other postoperative complications (including respiratory insufficiency and deep sternal infection). No one in group N suffered perioperative stroke. One patient in group A who underwent CABG with on-pump beating had a late stroke (watershed lesion infarction) 6 days after surgery. This was due to low perfusion. No cerebral infarction or neurologic defects occurred in OPCAB.

### Table 1  Patient preoperative demographics

<table>
<thead>
<tr>
<th></th>
<th>Group N (n = 183)</th>
<th>Group A (n = 42)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>69.8 ± 8.9</td>
<td>75.3 ± 5.5</td>
<td>p &lt; 0.01</td>
</tr>
<tr>
<td>&gt; 75 years old</td>
<td>68 (37.2%)</td>
<td>26 (61.9%)</td>
<td>p &lt; 0.001</td>
</tr>
<tr>
<td>Sex (male)</td>
<td>132 (72.1%)</td>
<td>35 (83.3%)</td>
<td>NS</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>72 (39.3%)</td>
<td>18 (42.8%)</td>
<td>NS</td>
</tr>
<tr>
<td>Hemodialysis</td>
<td>9 (4.9%)</td>
<td>4 (9.5%)</td>
<td>NS</td>
</tr>
<tr>
<td>Poor LVEF (&lt;50%)</td>
<td>24 (13.1%)</td>
<td>6 (14.3%)</td>
<td>NS</td>
</tr>
<tr>
<td>Logistic EuroSCORE</td>
<td>3.16 ± 2.2</td>
<td>5.39 ± 2.9</td>
<td>p &lt; 0.001</td>
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LVEF, left ventricular ejection fraction

### Table 2  Surgical characteristics

<table>
<thead>
<tr>
<th></th>
<th>Group N (n = 183)</th>
<th>Group A (n = 42)</th>
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<tbody>
<tr>
<td>Intra operative IABP</td>
<td>30 (16.4%)</td>
<td>2 (4.8%)</td>
</tr>
<tr>
<td>Conventional CABG</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>On-pump beating</td>
<td>7 (3.8%)</td>
<td>6 (14.3%)</td>
</tr>
<tr>
<td>Axillary artery cannulation</td>
<td>0 (0%)</td>
<td>4 (9.5%)</td>
</tr>
<tr>
<td>OPCAB</td>
<td>176 (96.2%)</td>
<td>36 (85.7%)</td>
</tr>
<tr>
<td>Aorta no-touch technique</td>
<td>74 (40.4%)</td>
<td>27 (64.3%)</td>
</tr>
<tr>
<td>Total distal anastomoses</td>
<td>3.0</td>
<td>2.6</td>
</tr>
</tbody>
</table>

IABP, intra aortic balloon pumping; CABG, coronary artery bypass grafting; OPCAB, off-pump coronary artery bypass
patients (n = 212). No hospital death occurred in either group during the study period.

**DISCUSSION**

This study showed a significant association between severe atherosclerotic disease and increased incidence of postoperative complications, but not perioperative stroke. Our data suggest that severe atherosclerosis was associated with peripheral circulatory failure and deep sternal infections. Use of axillary artery cannulation, OPCAB, and the no-touch aorta technique reduced morbidity and mortality in those with severe atherosclerosis.

OPCAB has gained worldwide popularity and is associated with fewer postoperative complications and shorter lengths of stay in the hospital or intensive care unit than conventional CABG. Nonrandomized studies report significant reductions in mortality and major neurologic events with OPCAB. In a comparison of OPCAB and conventional CABG, Mack et al. demonstrated that the elimination of CPB improved early survival in CABG patients, with a significant difference in mortality between the OPCAB and conventional CABG groups (1.9% vs. 3.5%). Other studies that compare OPCAB and conventional CABG also show that use of OPCAB in patients with severe atheromatous aortic disease is associated with significantly lower mortality, perioperative stroke, and overall complications. A recent case-matched report demonstrated a hospital survival benefit in specific high-risk OPCAB patients. These findings are consistent with our outcomes.

Severe atherosclerosis of the ascending aorta and arch is known to increase the risk of mortality and perioperative stroke in CABG patients. In a recent review of more than 35000 patients, the stroke rate ranged from 0.9%—3.9% after isolated CABG, with a mean rate of 2%; stroke mortality ranged from 13%—25%. Data show that the incidence of stroke remains high in patients with moderate or severe ascending aortic disease when CPB (guided by epiaortic scanning) and minor modifications in surgical strategy are used, and that mortality is excessive (24.8%) in patients who have a stroke. Calafiore et al. noted that limited or no manipulation of the ascending aorta in patients with severe atheromatous aortic disease is important. We found that avoiding CPB and manipulation of the aorta improved outcomes in this subset of high-risk patients.

We routinely use intraoperative epiaortic scanning to identify atheromatous aortic disease in all patients scheduled to undergo CABG. If atheromatous aortic disease is present, we use a no-touch technique for the aorta with OPCAB, or axillary artery cannulation and on-pump beating with CPB. These can be accomplished using in situ arterial grafts. In this study, identification of atherosclerosis of the ascending aorta by preoperative examination or intraoperative epiaortic scanning prompted the use of the aorta no-touch technique in 27 of 42 patients (64.3%). Wareing et al. reported that when conventional CPB was used, the stroke rate was 1.1% in patients with normal or mild atherosclerosis, 3.0% in moderate cases, and 4.8% in those with severe atherosclerosis. These findings indicate that intraoperative screening of the ascending aorta might reduce the incidence of perioperative stroke.

It is not clear which options—avoiding CPB, avoiding aortic manipulation and proximal anastomosis, or eliminating CPB and aortic manipulation—might reduce the incidence of perioperative stroke. However, we had zero mortality using CPB, even in patients undergoing CABG under the on-pump beating. This suggests that CPB is not an independent risk factor for complications or mortality.

The proportion of strokes caused by aortic atheroemboli rather than concomitant cerebral atherosclerotic disease has not been clearly defined. However, data show that use of varied surgical techniques can reduce the incidence of perioperative stroke. Depending on the location of the disease, varied surgical techniques have included a no-touch technique for the ascending aorta,

<table>
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<tr>
<th>Table 3 Complications and mortality</th>
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<tr>
<td><strong>Group N (n=183)</strong></td>
</tr>
<tr>
<td>-----------------------------------</td>
</tr>
<tr>
<td>Postoperative atrial fibrillation</td>
</tr>
<tr>
<td>Prolonged respiratory failure</td>
</tr>
<tr>
<td>Deep sternal infection</td>
</tr>
<tr>
<td>Stroke</td>
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<tr>
<td>In-hospital mortality</td>
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use of \textit{in situ} arterial grafts, and modifications in sites of cannulation and proximal anastomoses. In this study, tailoring the surgical strategy to the results of cerebrovascular and aortic evaluations reduced morbidity from CABG-associated perioperative stroke.

Nakamura et al.\textsuperscript{19)} found that intensive management of cerebral hemodynamics and atheromatous aorta reduced perioperative stroke in CABG patients. Prophylactic cerebrovascular interventions reduced stroke risk in those with poor cerebral perfusion reserve due to cerebrovascular atherosclerosis. We performed single photon emission computed tomography (SPECT) in a few patients in group A. One underwent superficial temporal artery to middle cerebral artery (STA-MCA) bypass, and another preoperative stent deployment in the carotid artery. No prior studies have shown any significant effect of STA-MCA bypass in preventing a subsequent stroke,\textsuperscript{20)} but the patient who underwent it prior to CABG did not suffer a stroke.

OPCAB techniques have recently been improved. Although cardiac output can be reduced during bypass of the left circumflex arteries, hypotension during anastomosis or conversion to CPB is rare. Nakamura et al.\textsuperscript{19)} reported on the use of OPCAB without bypass of the diseased left circumflex arteries due to low aortic pressure. In this study, we safely performed off-pump coronary revascularization of the circumflex area using our original techniques and instruments, resulting in complete revascularization.

Moazami et al.\textsuperscript{21)} reported that acute thrombosis may occur after cardiac surgery at the site of preexisting intracranial artery disease, but the administration of postoperative heparin did not independently reduce the risk of perioperative stroke. Perioperative management of aspirin therapy in patients undergoing coronary artery bypass surgery varies among surgeons and across medical institutions. Studies indicate that discontinuation of aspirin therapy before CABG is associated with reduced mortality, without significant increases in hemorrhage, blood product requirements, or related morbidities.\textsuperscript{22, 23)} We continued perioperative antiplatelet therapy (aspirin, ticlopidine [Ticlid; Roche Laboratories, Nutley, New Jersey, USA] or clopidogrel), and administered postoperative heparin to all patients until their PT-INR was $>1.7$.

Increased thrombogenicity and fluctuating blood pressure due to postoperative low output syndrome or atrial fibrillation are potential mechanisms of late stroke.\textsuperscript{24)} Further studies of postoperative anticoagulation are needed to determine optimal strategies for preventing the thrombotic occlusion of preexisting intracranial arterial stenosis.

**Limitations**

The limitations of this study include its small sample size, the use of retrospective patient data, the absence of a control group, and the fact that no patients underwent CABG using conventional on-pump techniques. Intensive management of cerebral vascular disease may have been useful, but was not performed because of increased cost. The strength of this study was the lack of a learning curve for OPCAB surgery; only a few experienced surgeons have been performing by the unified techniques since 1999.

**Conclusions**

Although there was no mortality among patients undergoing elective isolated CABG, postoperative morbidity (deep sternal infection and stroke) was higher in those with severe atherosclerotic disease than in those without it. Data suggest that we can prevent perioperative stroke and minimize neurologic complications by tailoring surgical strategies (e.g., use of OPCAB, the aorta no-touch technique, or axillary artery cannulation) in patients with severe atherosclerosis.

Preoperative vascular evaluation and tailored surgical strategies (various surgical techniques and perioperative drug management; antiplatelet and anticoagulation therapy) are critical to prevent complications, such as cerebral infarction, and to improve outcomes after CABG. Nonetheless, other complications in patients with severe atherosclerosis remain a problem. Therefore, we suggested that perioperative blood glucose control and respiratory management become the most important to prevent other complications in patients with very severe atherosclerosis. Further studies are required to determine the costs and benefits of a more aggressive approach to preoperative vascular evaluation in patients requiring CABG.

**References**


2) Davila-Roman VG, Murphy SF, Nickerson NJ, Kou-


